UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,200	04/22/2005	Chaim Springer	030231-0156	8842

22428 7590 01/20/2010

FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
CORNET, JEAN P	

ART UNIT	PAPER NUMBER
1628	

MAIL DATE	DELIVERY MODE
01/20/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,200	SPRINGER ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-13* is/are pending in the application.

4a) Of the above claim(s) *14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 9/30/2009 in response to the Non-Final office Action of 10/05/2009 is acknowledged and has been entered.

Claims 8-14 are pending and claim 8-13 are under current examination. Claims 1-7 and 15 are canceled by Applicant.

Rejection withdrawn:

Claim Rejections - 35 U.S.C. § 112 2nd paragraph/35 U.S.C. § 101

2. Applicant's arguments, see page 5, filed 10/05/2009, with respect to the 35 U.S.C. § 112 2nd paragraph/35 U.S.C. § 101 have been fully considered and are persuasive. The rejection of claim 15 has been withdrawn due to cancellation of the claim.

Rejections Maintained:

Claim Rejections - 35 USC § 103

Claims 8-13 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Avital et al.,("charcoal is a Sensitive, Specific, and stable Marker for the Diagnostic of Aspiration in Hamsters", Pediatric Research, March 2002, pp. 397-401, Vol. 51, No. 3,) cited in the 892 form in view of and Joon et al. (Assessment of

Biodegradability of polymeric Microspheres in vivo: Poly(DL-lactic acic), and poly(L-lactic acid) and poly(DL-lactide-co-glycolide) microspheres, Arch. Pharm. Res. Vol 16, No. 4, pp. 312-317, 1193"), cited in the 892 form .

3. As to claims 8 and 9, Avitar et al. teaches a diagnostic composition for detecting aspiration by Instillation of charcoal particles in trachea of hamsters. Instillation of activated charcoal particles mixed with milk was compared with instillation of normal saline or milk in hamsters and the charcoal particles were identified in bronchoalveolar lavage fluid and alveolar macrophages for a period of 3 months. The charcoal particles were made from an inert non-harmful material and are used as a sensitive, specific and stable marker for the diagnosis of aspiration (page 397, right column). Avital et al. also teaches that aspiration can occur in children with neurologic impairment, but can be secondary to gastroesophaageal reflux and the administration of the charcoal particles can be given orally (page 397, left column). Furthermore, Avital et al teaches charcoal particles are too large and may retain within the lungs tissue for extended periods and behave as foreign bodies, inducing chronic inflammatory response and may not be safe as a diagnostic tool for humans (last 3 lines, right column, page 400 and 401 bridging).

Avital et al does not teach a diagnostic composition comprising administering biodegradable polyester microspheres (polylactic acid) having 0.1-10 microns, but suggests that particles that are small in size, inert, non-harmful and can be retained in the lungs tissue safely for extended period could help in the diagnosis of aspiration.

As to claims 10-13 and 15, Joon teaches non toxic, non-tissue reactive biocompatible and biodegradable polyester microspheres such as PDLA poly(Dl-lactic

acid), PLLA poly(L-lactic acid) and PLGA poly(DL-lactide-co-glycolide) selected as model polymers as noble drug carriers of various drugs and their biodegradability was determined by analysis of magnetite content in the microspheres (page 312, second paragraph, right column). 3.93 microns-5.52 microns of the polyester microspheres were administered to mice and retained in their lungs (page 313, animal experiments). Particles ranging from 3 to 6 microns were mainly accumulated in the lungs and liver (page 314, second paragraph left column), due to their slow degradation (page 314, first paragraph, right column). The biodegradation of the copolymers is a function of the composition of lactic acid and glycolic acid. The recovery of the microspheres in the lungs was achieved by a magnet (page 316, first paragraph, left column).

Therefore, It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the Avital' s reference with that of Joon to administer an inert and non-harmful material, such as polyester microspheres as demonstrated by Avital in view of Joon, that can be retained in the lungs by inherent ingestion of alveolar macrophage for the detection of pulmonary aspiration having small and uniform particle size.

Although, Joon utilizes a magnet as a method of detection, however one of ordinary skill in the art would have recognized that other techniques such as broncholaveolar lavage would have also been able to perform the same task once the skill artisan in the art realizes polyester microspheres particles can be retained in the lungs, because Avital suggests obtaining bronchoalveolar lavage and detecting the

presence small, inert and non-harmful particles that can be retained in the lungs is a technique that has been used for the detection of particles in the lungs.

Because of the supporting properties of polyester microspheres, the scope of the claims is embraced by the teaching of the cited references.

One would have been motivated to do so; with a reasonable expectation of success to substitute the polyester microspheres as a sensitive and specific marker that could help diagnose aspiration, because they are safe, nonharmful, biodegradable and reliable. The techniques and skill required for making such substitution is conventional knowledge or well within the skill of ordinary artisan as microspheres have been used for a long time. One would have been motivated to combine the references and make the substitution because they are drawn to the same technical filed (constituted with the same ingredients and share common utilities, and pertinent to the problem which applicant concerns about./ MPEP 2141.01 (a).

All the critical elements required by the claims are obvious over the well taught and thus, the claimed subject matter is not patentably distinct over the prior art of the invention.

Applicant's arguments

4. In response to this rejection, Applicants assert the following:

A. Avital teaches the use of charcoal particles as a diagnostic marker in young children suffering from recurrent pneumonia and does not teach or suggest a method that substitutes charcoal particles with bio-degradable microspheres. In addition

Applicants argue that Joon fails to remedy the defects in Avital, although Joon discloses polymeric microspheres in which the focus is on assessing the factors that effect bio-degradaility and the rate of bio-degradability of polymeric microspheres. Hence Joon would not therefore be understood by a skilled artisan to teach a method for detecting pulmonary aspiration of gastroesophageal reflux. Therefore there is no motivation to combine Avital in view of Joon.

B. Applicants stated the Examiner is using impermissible hindsight to support the case of prima facie obviousness since Joon provides no teachings for the use of its polymeric particles as markers for detecting pulmonary aspiration and GER.

These arguments have been carefully considered, but are not found persuasive.

Response to Applicant's arguments

5. In response to Applicant's argument of part (A), Avital clearly suggest the use of charcoal particles as diagnostic marker for detecting aspiration, since aspiration can be secondary to gastroesphageal reflux besides from occurring in children with neurologic impairment. Applicants' specification discloses aspiration of food and gastric material into the tracheobronchial tree can result in a variety of disease states such as recurrent pneumonia, pulmonary fibrosis (page 1). Avital also teaches that charcoal particles are inert, non-harmful material and used as sensitive and stable marker as a detection method and are too large and may retain within the lungs tissue for extended periods and behave as a foreign bodies and inducing inflammatory response and may not be safe as a diagnostic tool for humans. Moreover, Joon discloses the polymeric

microspheres obtained by bronchoalveolar lavage, Joon suggests the detection of the bio-degradable polymeric microspheres was achieved by a magnet. In other words, these microspheres can be detected in lungs with other method of detection since they are safe, inert and non–harmful and can be retained in the lungs due to their slow degradation. The Examiner recognizes that it is the combination of all of the cited and relied upon references, which make up the state of the art with regard to the claimed invention. The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference and it is not that the claimed invention must be expressly suggested in any one or all of the references; but rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the present case, it would have been obvious to one of ordinary skill in the art to combine the reference and use the biodegradable polymeric microspheres taught by Joon vs. the charcoal particles of Avital to diagnose gastroesophageal reflux because as stated above charcoal particles are not safe and their large size may behave as foreign bodies and induce inflammatory response and polymeric microspheres are safe, inert material that are retained in the lungs One would have been motivated to do so; with a reasonable expectation of success to substitute the polyester microspheres as a sensitive and specific marker that could help diagnose aspiration, because they are safe, nonharmful, biodegradable and reliable..

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that

any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In this case the support the prima facie obviousness case was provided by Joon 's in vivo teachings as stated in the previous office action and above.

Conclusion

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on 571-272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Brandon J Fetterolf/

Primary Examiner, Art Unit 1642